Scientific Abstract

Prostate Specific Antigen (PSA) is a glycoprotein that was first identified in the prostate fluid more than 20 years ago (Carter et al, 1990 and Osterling, 1991). PSA is a unique tumor-associated antigen that presents a promising target for a cancer vaccine because it is produced exclusively by the prostate. By directing a strong cellular immune response against PSA, there is a potential to destroy tumor cells expressing this conserved antigen. In the proposed study, a plasmid encoding the PSA cDNA is injected intramuscularly into patients with the expectation of stimulating an immune response against cancerous prostate cells.

The mechanism of action for CNTO 23 is to generate an anti-PSA cellular immune response that will target PSA-expressing cells for destruction. Specifically, after CNTO 23 is injected into a subject, it will be taken up and expressed by muscle cells as well as by cells of the immune system. This will lead to the processing and presentation of PSA antigen by lymphoid cells, and the generation of the cellular and humoral immune responses to PSA. The cellular response, with the generation of $CD8^+$ T-cells that specifically recognize PSA expressing cells and lyse them, is expected to be the effector of therapy.

The proposed trial represents a Phase I, open-label, dose-escalation, safety and efficacy study of repeated administration of CNTO 23 DNA vaccine. This study will enroll subjects with progressive or recurrent hormone refractory prostate cancer (HRPC) with castrate testosterone levels (0.3 ng/mL) and increasing PSA, with or without evidence of metastatic disease who have not previously received chemotherapy. Subjects will be enrolled sequentially into successive patient cohorts and immunized with escalating doses of cDNA plasmid until the highest dose level or the maximum tolerated dose (MTD) is reached. Patients with HRPC will be admitted into the study and receive intramuscular injections of the study drug every 2 weeks for the first 4 doses. The fifth dose will be administered 6 weeks after the fourth dose. The safety of the vaccine will be assessed as the primary objective of the study. Responses and progression of measurable disease and surrogate markers, palliation for those on medication for disease-related pain, measures of immunologic response to the vaccine, and survival will be assessed as secondary endpoints of this study.